Supplemental Materials: Dual Targeting with Cell Surface Electrical Charge and Folic Acid via Superparamagnetic Fe_3O_4@$Cu_{2-x}S$ for Photothermal Cancer Cell Killing

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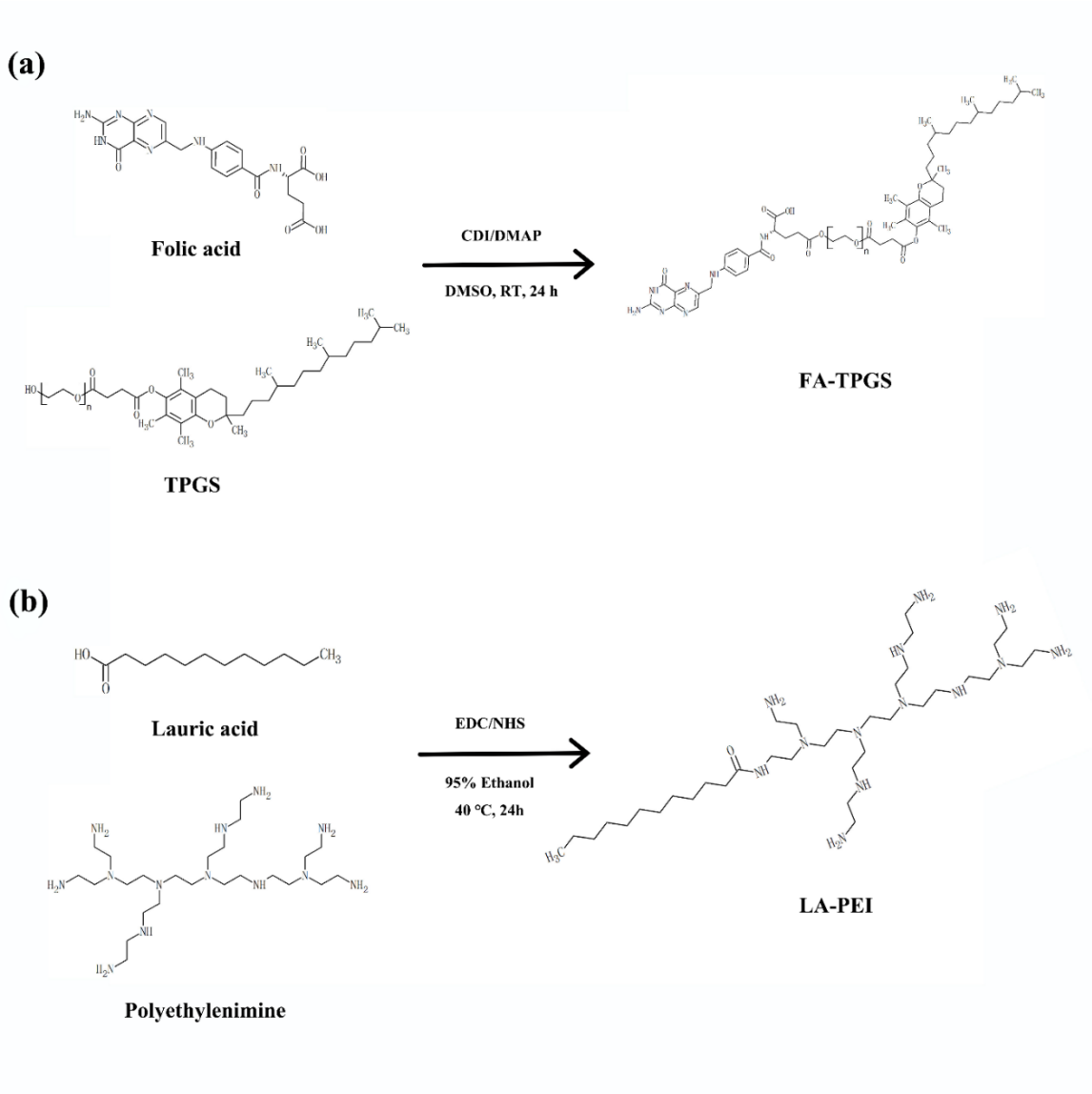

Figure S1. The chemical structures and synthesis procedures of (**a**) FA-TPGS and (**b**) LA-PEI.

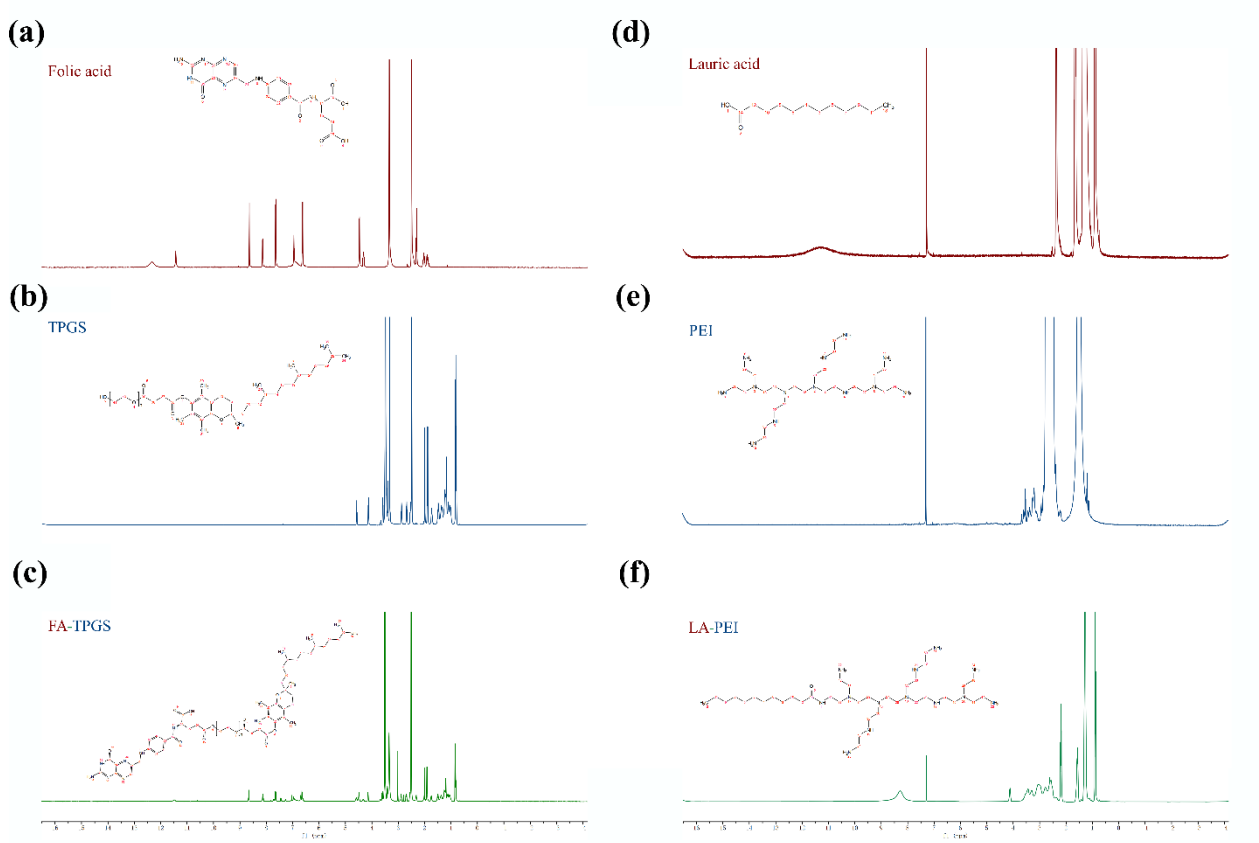

Figure S2. ^{1}H-NMR characterization of the coating polymers (**a**) Folic acid, (**b**) TPGS, (**c**) FA-TPGS in DMSO-d6, (**d**) Lauric acid, and (**e**) PEI, and (**f**) LA-PEI in Chloroform-d.

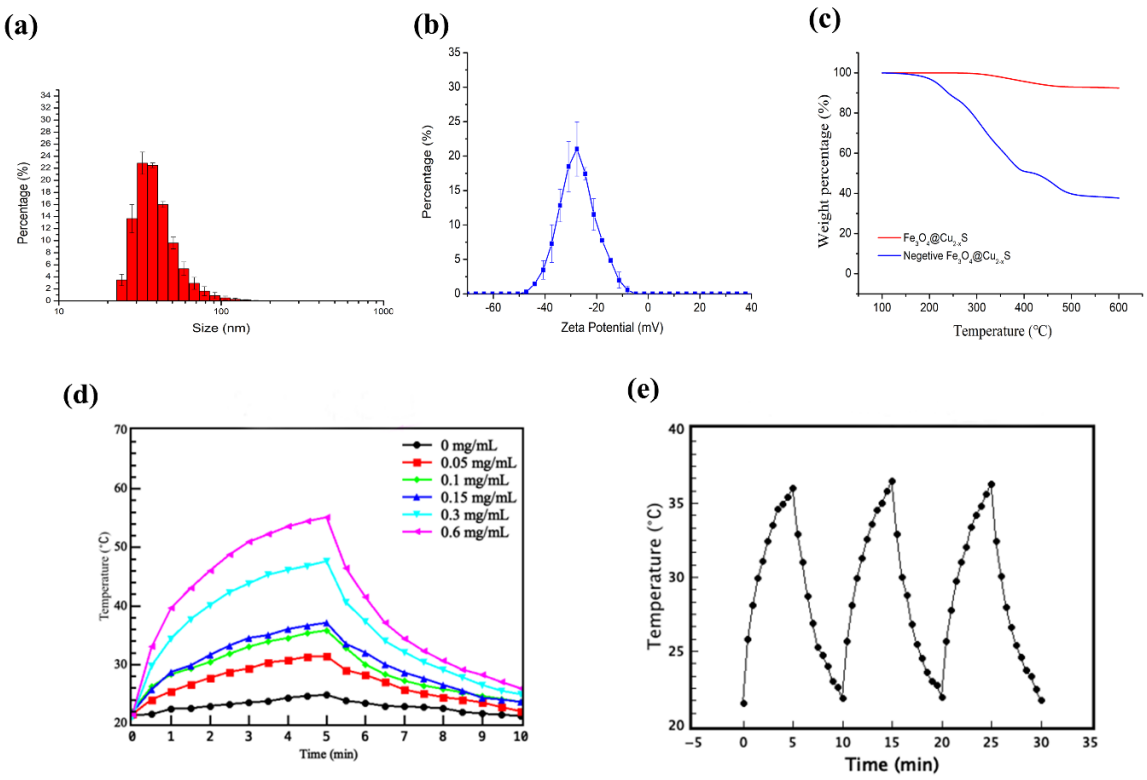

Figure S3. (**a**) Size distribution of the negative Fe_3O_4@$Cu_{2-x}S$ nanoparticle, (**b**) surface zeta potential of negative Fe_3O_4@$Cu_{2-x}S$, (**c**) thermogravimetric analysis (TGA) curves of uncoated Fe_3O_4@$Cu_{2-x}S$ and negative Fe_3O_4@$Cu_{2-x}S$, (**d**) temperature vs.

time curves for negative $Fe_3O_4@Cu_{2-x}S$, and (**e**) temperature vs. time curves of negative $Fe_3O_4@Cu_{2-x}S$ for three on/off cycles.

Table S1. Photothermal conversion efficiencies of negative $Fe_3O_4@Cu_{2-x}S$, PEI-$Fe_3O_4@Cu_{2-x}S$, and FA-PEI-$Fe_3O_4@Cu_{2-x}S$ at concentration of 0.15 mg/mL.

	FA-PEI-Fe_3O_4	Negative $Fe_3O_4@Cu_{2-x}S$	FA-PEI-$Fe_3O_4@Cu_{2-x}S$
η	22.99	16.46	52.17

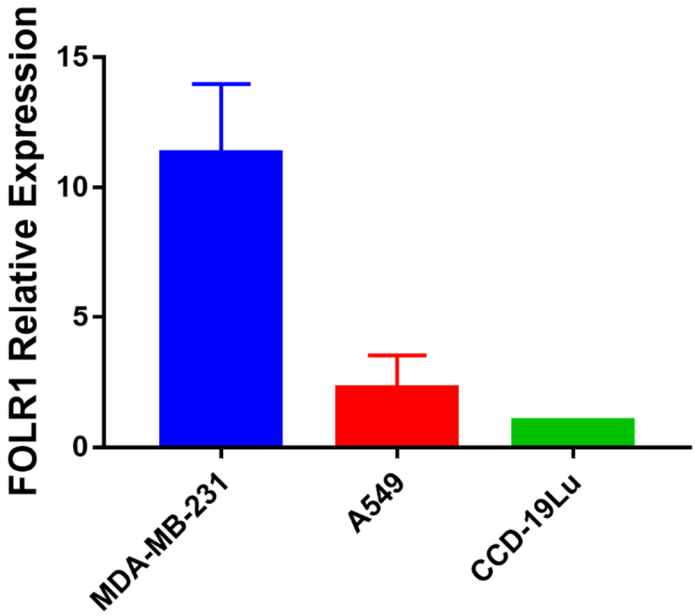

Figure S4. FOLR1 expression levels in different cell lines. Human *FOLR1* mRNA levels in tumor cells were measured by qRT-PCR and normalized to Beta-Actin mRNA.

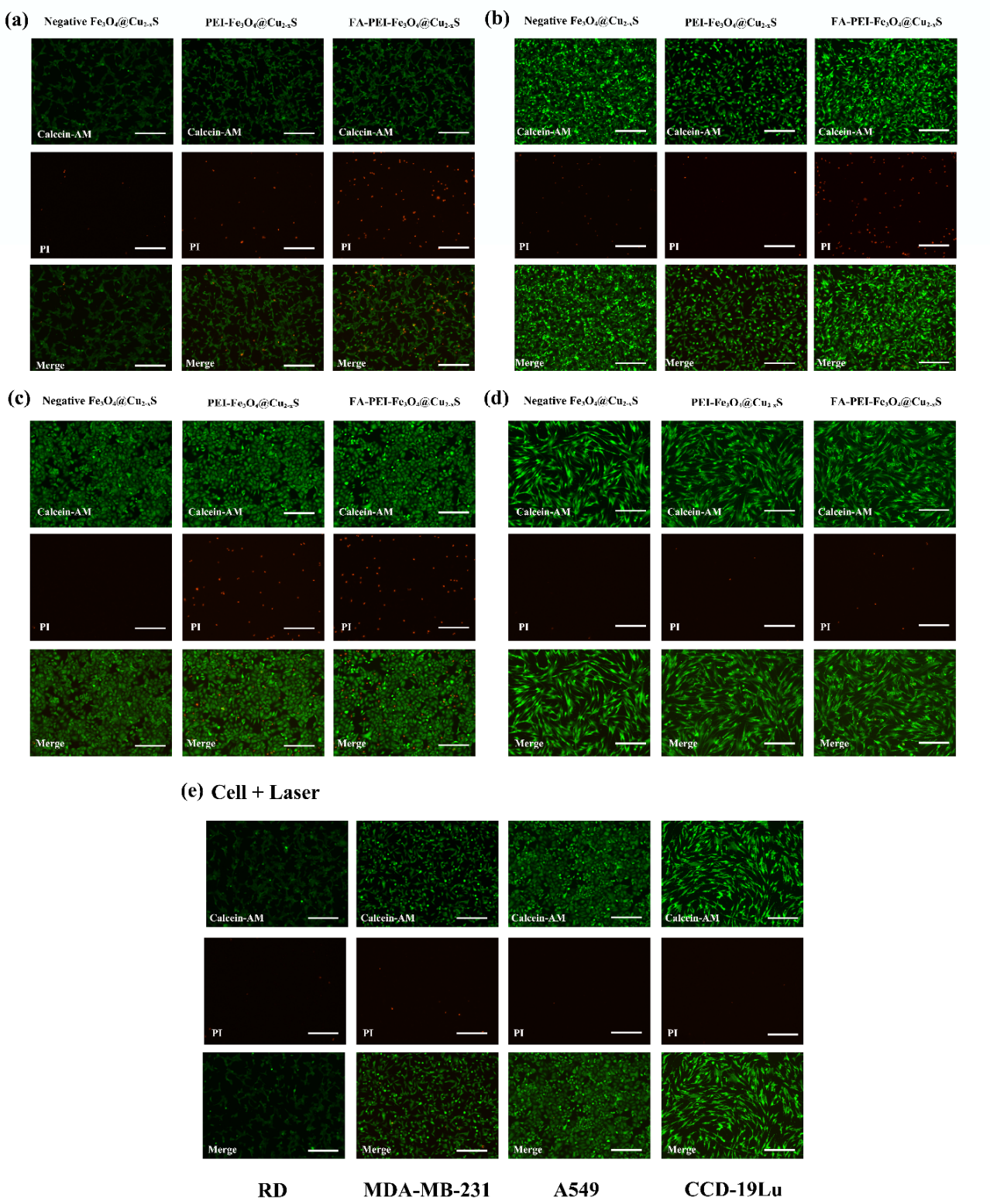

Figure S5. In vitro toxicity of negatively-charged $Fe_3O_4@Cu_{2-x}S$, positively-charged PEI- $Fe_3O_4@Cu_{2-x}S$, and FA-PEI-$Fe_3O_4@Cu_{2-x}S$ at 0.32 mg/mL on (**a**) RD 769 cell line, (**b**) MDA-MB-231 cell line, (**c**) A549 cell line, (**d**) CCD-19Lu cell line without laser, and (**e**) 5 minute 2 W cm^{-2} 808 nm laser irradiation treatment for different cells without nanoparticle. Scale bar: 275 μm.

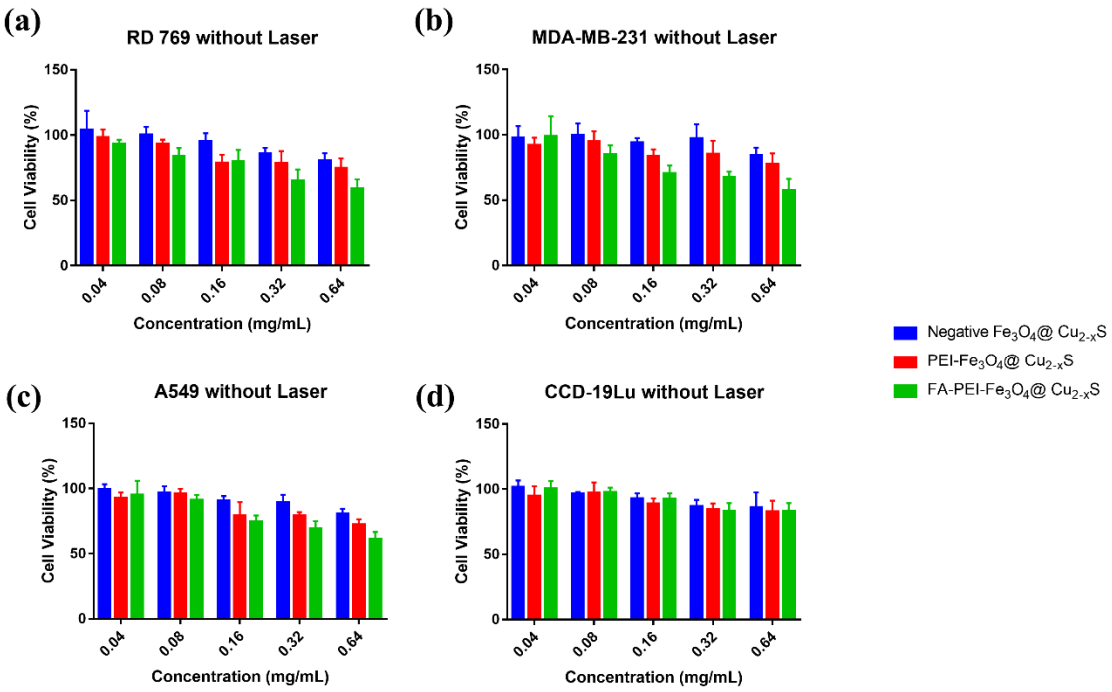

Figure S6. Cell viability vs. concentration of different nanoparticles for cancer cells (**a**) RD 769, (**b**) MDA-MB-231, (**c**) A549 and (**d**) non-malignant CCD-19Lu cells without laser treatment.